California Institute for Regenerative Medicine

Combinatorial Platform for Optimizing Microenvironments to Control hESC Fate

Grant Award Details

Combinatorial Platform for Optimizing Microenvironments to Control hESC Fate

Grant Type:	SEED Grant
Grant Number:	RS1-00173
Investigator:	**Name:** Shu Chien **Institution:** University of California, San Diego **Type:** PI
Human Stem Cell Use:	Embryonic Stem Cell
Award Value:	$577,148
Status:	Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Combinatorial Platform for Optimizing Microenvironments to Control hESC Fate

Public Abstract:

The aim of California Stem Cells Initiative is to develop new therapeutical approaches by utilizing human embryonic stem cells (hESCs) to renew themselves and to differentiate into a variety of cell types, thus enabling the engineering of specific tissues to treat diseases that cannot be currently cured. To realize the potential of hESCs in regenerative medicine will require (1) the establishment of conditions for the expansion of these cells into a sufficiently large quantity and (2) the development of protocols to differentiate them into specific cell types and generate the desired tissues. Experimental manipulation of the environmental cues, such as chemical signals and physical stresses, to which stem cells are exposed, will lead to the discovery of conditions that specifically direct hESC growth and differentiation.

Studies on factors affecting stem cell growth and differentiation tend to focus on one or a few elements in the microenvironment, e.g., some proteins in the matrix underlying the cell or growth factors brought to the cell from the circulation or neighboring cells. The proposed research will develop a platform that will allow the concomitant screening of thousands of conditions consisting of combinations of various molecules for the systematic selection of the optimum conditions for hESC growth and differentiation. This platform is based on a microarray technology using robots to place 1200 spots of individual and combinations of proteins in a precise pattern on a glass slide surface. The hESCs attached to these spots will interact with different molecules in the patterned spots to elicit specific cellular responses. In addition, we will subject the cells on the arrays to well-controlled mechanical forces imposed by fluid shearing. Thus, we will combine mechanical and molecular stimuli in a controlled manner to study the responses of hESCs to physicochemical modulations in their microenvironment in terms of their signaling behavior and cellular fate, i.e., growth and differentiation.

The application of hESCs for regenerative medicine requires the establishment of the optimal physicochemical microenvironment that allows us to control and direct the growth and differentiation of these cells. Our proposed research focuses specifically at this critical need. We will develop a 'systems' approach to understanding the response of hESCs to multiple factors in the microenvironment. The results will lead to the definition of the optimal microenvironment parameters for the control of differentiation of hESCs into specific cell types such as cardiovascular cells, neuron cells, cartilage/bone cells, etc., for the treatment of many important human diseases. Hence, this project has fundamental importance and broad applications. This is a most cost-effective way to pursue hESC research for the improvement of human health and quality of life, and the resulting technology advances may provide financial gain for the people in California.

Statement of Benefit to California:

Millions of people suffer from diseases and injuries that cannot be cured by current treatments in clinical medicine, e.g., cancer, heart diseases, Alzheimer's diseases, Parkinson's diseases, and spinal cord injury. Recent knowledge of the potential of the pluripotent stem cells has opened the door of regenerative medicine, which will enable scientists/physicians to develop new strategies for treating patients with cell-based therapies to overcome the inadequacy of the conventional chemistry-based treatments. Most current stem cell research studies focused on the pathogenesis of a single disease, aiming at improving the treatment of the disease. Success of such research activities requires a platform that can control and direct the fate of the stem cells in terms of proliferation and differentiation. The aim of our proposed research is to establish a platform that allows the systematic investigation of the role of the physicochemical microenvironment in modulating the fate of various types of stem cells. The result will provide a common foundation needed for stem cell research directed at a broad range of diseases.

Our proposed platform will allow the concomitant screening of thousands of parameters (separate or combinatorial) to select the optimal conditions for stem cell proliferation and differentiation. Thus, we will develop a 'systems' approach to understanding the response of human embryonic stem cells to the microenvironment. The results will lead to the definition of the optimal microenvironment parameters for the control of embryonic cell differentiation lineages, such as cardiovascular cells, neuron cells, or cartilage/bone cells, etc. With the modulation of the microenvirnment parameters at sublocations on a scaffold material, multiple cell types differentiation can be triggered from a single source of human embryonic stem cells, thus leading to the creation of the desired functional tissues to repair the degenerated organs.

About half of California's family suffered or will suffer from degenerated diseases and injuries. The results from our proposed studies, by providing the fundamental knowledge on how to manipulate human embryonic stem cell fate, will significantly facilitate stem cell research for virtually all diseases. The success of stem cell-based therapies will markedly reduce the future health care cost and ease the financial burden of California residences. In addition, the outcome of this project will lead to the development of a biotechnology platform to provide benefits to the advancement of California biotechnology. The patents, royalties and licensing fees that result from the advances in the proposed research will provide California tax revenues. Thus, the current proposed research provides not only the essential foundation for the scientific advances in regenerative medicine to improve human health and quality of life, but also potential technology advancement and financial profit for the people in California.
